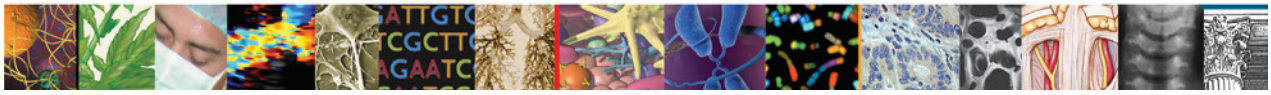

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Perspective

# Antigenic Drift and Antivaccine Shift in the 2025–2026 Influenza Season

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Recent headlines about influenza have reported a "super flu" causing a "record-breaking season" that is "overwhelming hospitals." Although less dramatic, data from the Centers for Disease Control and Prevention (CDC) reveal substantial influenza activity: the agency estimated that there were more than 20 million cases of influenza illness, 270,000 influenza-related hospitalizations, and 11,000 deaths from influenza in the United States through January 24, 2026. These numbers aren't extraordinary as compared with those from previous seasons, but some indicators of influenza activity and severity have been remarkable.

Outpatient visits for influenza-like illnesses reached their highest level in nearly three decades, driven largely by pediatric visits. During the week ending on December 27, 2025, hospitalization rates for children rose to their highest weekly level since 2009 and were higher than the rate during the peak of the 2009–2010 influenza A(H1N1) pandemic season. As of January 24, 2026, a total of 52 influenza-associated pediatric deaths had been reported to the CDC; by comparison, 47 such deaths were reported at a similar time in the 2024–2025 influenza season, during a severe season with a total of 289 pediatric deaths. In mid-January, the CDC classified the severity of the 2025–2026 influenza season as moderate in general and high in the pediatric age group.

What explains the intensity of influenza activity during the 2025–2026 season? Both viral and host factors are involved. Some of these factors can be managed, whereas others are largely beyond human control. Influenza viruses are constantly changing; their genes mutate by means of "antigenic drift," allowing them to partially evade host immunity associated with previous vaccination or infection. Antigenic drift is distinct from "antigenic shift," in which an influenza A virus undergoes an abrupt, substantial change, typically by means of genetic reassortment, creating a new strain for which there is little or no preexisting population immunity and therefore the potential for pandemic spread.

This season, the effects of antigenic drift are being felt throughout the world, with high numbers of cases having been reported in a short period. This surge can be attributed to an influenza A(H3N2)

virus that has several adaptations to the hemagglutinin protein on its surface. The emerging variant, subclade K (also known as J.2.4.1), was first recognized by the CDC in June 2025.[1] Large outbreaks of subclade K occurred in Australia and New Zealand in August and in the United Kingdom and Japan in the fall. Subclade K has been the predominant circulating virus in the United States this winter, accounting for more than 90% of subtyped H3N2 viruses.

The rise of subclade K came several months after the selection of the influenza strains used for the northern hemisphere influenza vaccine. Because current vaccine technologies relying on egg production require substantial lead time, viruses must be chosen 6 months before planned vaccine distribution. With H3N2's drift, hosts are at a disadvantage. Immune factors associated with previous influenza infections or vaccinations won't be well matched to the new variant. This season's vaccine is anticipated to be less protective than the vaccines administered in years when viruses changed little between strain selection and the influenza season. Data from studies using antisera from ferrets immunized with the 2025–2026 vaccine strains were in keeping with this expectation. Nonetheless, preliminary population vaccine-effectiveness data from the United Kingdom suggest that this year's vaccine provides similar protection against emergency department visits and hospitalizations for influenza A(H3N2) as vaccines have in recent years.[2]

Variables related to viral and host biology aren't the only factors driving high levels of influenza activity; shifts in host behavior have also contributed. Influenza-vaccination rates have decreased in the United States as antivaccine sentiment has become more common. In a recent KFF–Washington Post survey, only 65% of U.S. parents said they were confident that influenza vaccines are safe for children.[3] At the same time, the U.S. government has substantially scaled back efforts to encourage influenza vaccination. The CDC's successful "Wild to Mild" influenza-vaccination campaign — designed to highlight the vaccine's ability to prevent severe disease — was discontinued in early 2025. The agency's activities for the annual National Influenza Vaccination Week, held each year during early December, were also curtailed this season. In addition, routine broadcast and social media content from the CDC recommending vaccination during influenza season has been scaled back.

Vaccine acceptance has dropped in recent years because of fatigue associated with the Covid-19 pandemic and antivaccine messaging, and recent changes to the influenza program will probably further fuel this trend. Among children between 6 months and 17 years of age, the cumulative influenza-vaccination coverage rate was 45.1% as of January 17, 2026, as compared with 57.4% for the same week during the 2019–2020 season. As of January 10, 2026, a total of 133.49 million doses of influenza vaccines had been distributed in the United States, as compared with 145.54 million doses during the same week in the 2024–2025 season and 172.97 million doses in the 2019–2020 season. Although more vaccines are distributed than administered, distribution is often used as a proxy for vaccine demand.

Influenza causes a substantial number of hospitalizations and deaths in the United States each year, and influenza viruses will continue to evolve. Given this reality, what actions can the medical, scientific, and public health communities take to address the virus's antigenic-drift advantage in the future?

First, there is a need for stronger global virus surveillance. Early detection of emerging influenza-virus strains is essential for strain selection for vaccines. The United States' withdrawal from, and cessation of support for, the World Health Organization threatens the CDC's access to virus samples and could lead to fewer candidate strains being available to consider for next season's vaccine.

Second, better vaccines could be developed. New technologies, especially mRNA platforms, can shorten the time between strain selection and vaccine availability by multiple months, permit increased vaccine production, and improve the correlation between circulating viruses and vaccines. A recent clinical trial published in the *Journal* showed that an mRNA influenza vaccine had higher relative efficacy against influenza than vaccines made using traditional egg-based technology, albeit being associated with more reactogenicity events.[4] Yet instead of further exploring these technologies, the U.S. Department of Health and Human Services (HHS) canceled $500 million in funding for mRNA-vaccine research and development in August 2025. Although a fraction of this funding is being covered by the Coalition for Epidemic Preparedness Innovations, HHS's decision undermines the response to seasonal influenza and will leave the United States more vulnerable to the next influenza pandemic.

Finally, it will be essential for

more people, not fewer, to get vaccinated against influenza. It is a truism that "vaccines don't save lives — vaccinations do." Rather than working to reduce the burden of influenza during the current season, HHS, under Secretary Robert F. Kennedy, Jr., has taken steps to increase mistrust in vaccines. By altering content on the CDC's website to cast doubt on the safety of vaccines, promoting unfounded associations between vaccines and autism, and removing the recommendation for routine influenza vaccination from the federal childhood immunization schedule, Kennedy and HHS have sowed confusion among patients, parents, and clinicians. These changes also increase barriers to vaccination for people who want to get vaccinated against influenza. Decreased rates of vaccination will increase the risk of illness, hospitalization, and death during this influenza season and future seasons.

Although indicators showed reductions in the intensity of influenza activity in the first half of January 2026, it is difficult to predict what will happen during the remainder of the 2025–2026 influenza season. What is clear is that influenza viruses will continue to adapt to evade immunity — antigenic drift is inevitable. What is not inevitable is the low level of support the U.S. government has directed to collaborative global virus surveillance, new vaccine technologies, and promotion of vaccine uptake. Modeling data have shown that small increases in vaccine effectiveness or vaccine coverage can lead to substantial reductions in influenza burden.[5] By increasing surveillance, taking advantage of new technologies to make better vaccines, and improving vaccine coverage, the United States could substantially reduce influenza-related hospitalizations and deaths. We can do better. Will we?

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